Asian Journal of Pharmaceutical Education and Research
Vol -12, Issue-3, July- September 2023
ISSN:2278 7496

RESEARCH ARTICLE Impact Factor: 7.014

An Experimental Study of Analgesic Activity of Selected Drugs in Comparison with Conventional NSAIDS

Sireesha Kalva*, Ramyasree Yenni
Department of Pharmacology, Sri Venkateshwara college of Pharmacy, Osmania University Madhapur.
*Corresponding Author's E mail: sireesha.kalva@gmail.com
Received 22 May 2023; Revised 28 May 2023; Accepted 21 June 2023, Available online 15 July 2023.

Cite this article as: Kalva S, Yenni R. An Experimental Study of Analgesic Activity of Selected Drugs in Comparison with Conventional NSADIDS. Asian Journal of Pharmaceutical Education and Research. 2023; 12(3): 74-80.
https://dx.doi.org/10.38164/AJPER/12.3.2023.74-80

ABSTRACT
Pain is an unpleasant sensation but a protective mechanism of our body. It is the most common medical complaint requiring a visit to a physician. The new non-steroidal anti-inflammatory drugs [NSAIDS] are commonly used. Healthy adult Swiss albino rats are used as experimental animals. The analgesic activity of the selected drugs were evaluated using eddy hot plate method. Rats weighing 200-250gm of either sex were divided into 6 groups. Oral diclofenac is used as standard and water for injection is used as control. Etoricoxib, Atorvastatin, Triphala and Aloe Vera are used as test drugs. The present study was conducted to evaluate and compare the anti-nociceptive activity of different selected drugs with conventional NSAIDS diclofenac in a hot model of acute pain using hot plate tests. In comparison with control group [vehicle] diclofenac showed significant increase in the reaction time at various time periods in the hot plate tests. In the hot plate model, the test drugs [etrocoxib, atorvastatin, Triphala and aloe Vera] showed a significant increase in the reaction time in comparison to control group. Our study concludes that various drugs selected etoricoxib, atorvastatin, triphala and aloe Vera have therapeutic potential for treating pain disorders and is non inferior to standard drug- Diclofenac.

Keywords: Analgesic activity, eddy's hot plate, albino rats, Diclofenac sodium, Etoricoxib.

INTRODUCTION

Pain is the subjective, unpleasant sensations that go along with damage or near damage to tissues. Chemicals released nearby as a result of cell injury either produces pain by direct stimulation or by stimulation of nerve endings responsible for the mediation of pain[1]. Pain involves complicated pathophysiology. Peripheral stimulation of nociceptors by low pH, Substance P, histamine, bradykinin and most importantly PGs and leukotrienes plays a key role[2]. Along with pain pathway there are opioid receptors and monoaminergic pain modulating circuits that play role in pain modulation[3].

Pharmacological management of pain requires the use of analgesic drugs [4]. COX inhibitors are an integral part of most analgesics regimens, COX enzymes exist in two forms, COX-1 and COX-2. COX-1 form is

constitutive and COX-2 is inducible and synthesizes prostanoids that mediate inflammatory process like pain, fever, tissue injury and infection. NSAID's reduce pain and edema by suppressing the formation of Prostaglandins (PG), by inhibiting the activity of the enzyme cyclooxygenase 1 and 2 (COX-1 and COX-2) [5]. For relief of pain and inflammation, non-steroidal anti-inflammatory drugs (NSAIDs) are the most commonly used treatment in three areas: inflammatory rheumatism, osteoarthritis and common pains, such as headache, trauma or minor tendonitis [4]. In addition, the damaging effect of some NSAID's upon the stomach and intestine is in part due to their acidic nature, as with indomethacin, ibuprofen, diclofenac, naproxene, aspirin, etc [6]. Their side effects as well as their therapeutic actions are related to their ability to inhibit cyclooxygenase enzymes involved in the first step of the arachidonic acid cascade [7,8]. However, prostaglandins are key mediators of several components of GI mucosal defense, so suppression of synthesis of prostaglandins (PGs) by NSAIDs greatly reduces the resistance of the mucosa to injury as well as interfering with repair processes. Selective COX-2 inhibitors were thought to be the solution to this conundrum as it is required that NSAIDs suppress prostaglandin synthesis at sites of inflammation, and not in the GI tract [9].

Etoricoxib is a selective COX-2 inhibitor. Selective COX-2 inhibitors elicit less GI damage and bleeding than conventional NSAIDs. India is a country with huge biodiversity of plants, out of them 1500 medicinal plants are well recognized which are serving the people ailments with fewer adverse reactions[10].

Aloe is made up of vast range of compounds. Aloe Vera gel exerts anti-inflammatory and analgesic properties. It has been utilized for reducing pain during dental treatments, mouth ulcers, sores, blisters, hemorrhoids and for wound healing in almost every parts of the world since ages [11, 12]. Thus we have undertaken this study to evaluate the analgesic property of the aqueous extract of Aloe Vera.

Triphala is a tridoshic formula of fruits of Terminalia belerica, Terminalia chebula and Emblica officinalis. Although mechanism of action is unclear it has got many pleotropic effects. Preliminary research work carried out with triphala has proved its efficacy as an anti-oxidant, immunemodulator, anti-aging, analgesic, anti-cancerous, anti-microbial and blood purifier [13, 14].

Osteoarthritis is a common disorder that causes severe pain and immobility in the patient. Treatment of osteoarthritis in modern medicine is currently limited to drugs that provide only symptomatic relief and these drugs are associated with serious adverse effects, considering various reports about anti-inflammator and analgesic activity of statins, it was evaluated for its analgesic activity.

MATERIALS AND METHODS

Selection of drugs:

For the purpose of this study the drugs selected are Diclofenac (conventional NSAIDs), Etoricoxib (Selective COX-2 inhibitor), Atorvastatin (Hypolipidemic drug), Triphala, Aloe Vera (Herbal drugs) and are obtained from Apollo pharmacy, Madhapur.

Experimental animals:

Adult Swiss Albino rats of either sex weighing 200-250gm were procured from authorized vendors. Rats were kept in propylene cages at a temperature of 25±2°C and relative humidity 45-55% with 12:12 light and dark cycle. Animals were given standard diet and water. Animals were acclimatized to the laboratory conditions 1-week before the experiment. Animals were fasted over night before the experiment. Experimental protocol was approved by the Institutional Animal Ethical Committee, IAEC was approval no. IAEC/SVCP/2022/02.

Acute toxicity studies

The toxicity of selected drugs on experimental animal was tested according to the Organization of Economic Co-operation and Development-423 guideline. Adult nulliparous and non-pregnant female albino rats were selected for the toxicity study, as female rats are more sensitive. Six animals were assigned to each group and fasted overnight prior to the administration of oral doses of test substances at a concentration of 5, 50, 300 and 2000 mg/kg body weight. All the test concentrations are adjusted to below 2 mL volume and administered using oral gavages. The animals were observed for first 30 min and periodically for 24 h. Mortality was not observed at any dose level. The observation was continued for 14 days for toxic signs.

Analgesic activity

Eddy's hot plate method

The rodent paws are very sensitive to the thermal stimulus, and they will show responses like jumping and licking when exposed to moderate heat. In this method, analgesic activity was tested against thermal stimulus. The rats are placed on the copper plate, which is at a temperature of 55°C-56°C and the time between initial placement and a hand lick or a jump was taken as reaction time. Rats are divided into six groups of six animals each. First group served as control and received normal saline (1ml). Group 2 received diclofenac (0.22mg). Group 3 received etoricoxib (1.7mg). Group 4 received atorvastatin (1.75mg). Group 5 received triphala (0.2mg). Group 6 received aloevera (0.22mg). The basal reaction

was noted at 0 min and then readings were taken at 30min, 60min, 90min, 120min and 180min after the treatment.

Statistical Analysis

Data were represented as mean ± standard error of mean and analyzed by one-way analysis of variance, followed by Dunnett's multiple comparison. $P < 0.05$ was considered as significant.

RESULTS AND DISCUSSION

The acute toxicity studies conducted on selected drugs did not reveal any toxic signs even at 1000 mg/kg (p.o) concentration. The experimental animals did not exhibit any behavioral changes. Hence, all the drugs were found to be safe for internal administration.

The analgesic activity of different concentrations of test solutions against thermal stimulus given by the hot plate are shown in table 1. Etoricoxib showed significant increase in the mean basal reaction time with a mean value of 11.8±0.770. When compared with control group at a dose of 1mg/kg at 120 min time. Atorvastatin dose has shown maximum analgesic action at 120 min with a mean value 7.3±0.541.

Triphala and aloevera at a dose of 1mg/kg also found to increase the mean reaction time siginificantly with a mean value of 11.8±0.820 and 7.6±0.365 at 180min respectively, when compared with control. The results obtained were also comparable to the standard drug diclofenac sodium. The selective cox-2 inhibitor etoricoxib has shown very significant result than diclofenac sodium 11.8±0.770 at 180min internal. The atorvastatin has also shown significant increase in the mean time maximum at 180mins with 7.3±0.541.

Diclofenac sodium was given to group II which has shown significant results compared to control group. The mean reaction time of control group at 0mins was found to be 8.3±0.541 and that of standard group II was found to be 2±0.282 and increase in the reaction time was noticed to be 7.8±1.073 at 120mins.
Hot plate method is well evaluated model for screening analgesics. Pain is centrally amended by a number of complex processes including opicate dopaminergic descending noradrenergic and serotonergic systems. The hot plate was preferred to examine the central anti-cociceptive activity since it had several advantages particularly the sensitivity to strong ant nociceptive and partial tissue damage. The analgesic effect produced by these experiments possibly will be through central mechanisms involving the receptors systems or peripheral inhibition of PGs and leukotrienes and other endogenous substance that are key players in pain.

Table 1: Effect of Selected Drugs on reaction time of rats in hot plate method.

Groups	0 Min	30 Min	60 Min	90 Min	120 Min	180 Min
Group I Control	8.3±0.541	8.5±0.836	8.5±0.4969	6.5±1.009	6.5±1.086	5.6±0.966
Group II Diclofenac	2±0.282[a]	2.5±0.616[a]	3±0.489[a]	4.1±0.820[a]	4.5±0.927[a]	7.8±1.073 [a]
Group III Etoricoxib	0.6±0.230[b]	1.3±0.541	2.3±0.783	3±1.019	4.5±0.469[c]	11.8±0.770[c]
Group IV Atorvastatin	2.8±0.658	3.5±0.787	4.3±0.365[c]	4.6±0.673	4.8±0.336[c]	7.3±0.541 [b]
Group V Triphala	2.6±0.541	2.8±0.594	4.8±0.522[c]	5.3±0.461	5.5±0.547[b]	11.8±0.820[b]
Group VI Aloe Vera	1±0.489[b]	1.6±0.230[b]	2.6±0.541	4.5±0.374[c]	5±0.4[c]	7.6±0.365

Hence in this research work was found that etoricoxib a selective cox-2 inhibitor is more effective than conventional NSAIDs and has low GI rate effect. Etoricoxib is a cox-2 inhibitor with high degree of selectively of its target. It produces an alternative to other selective and traditional NSAIDs in treating patients with arthritis and other painful conditions.

Osteoarthritis is a common disorder that causes severe pain and immobility in the patient. Treatment of osteoarthritis in modern medicine is currently limited to drug that provide only symptoms motor relief and these drugs are associated with serious adverse effects. Patients of hyperlipidemic are often overweight and more likely to suffer from osteoarthritis. It is evident from our research work that atorvastatin in spite of having hypolipidemic activity also possess analgesic activity which may be due to inhibition of bradykinin, tumor neurosis factor, IL-1b and chemokinins cxc which produce hyper nociception.

Herbal preparation could be an effective alternative in pain management. Herbal preparation after advantages over allopathic preparations by virtue of their stability over a period, safety, sustained availability, and fewer adverse effects. Our study is probably the initial step for evaluating analgesic activity of triphala. Analgesic activity of triphala could probably be because of the inhibition of effect of the release of endogenous substances that excite afferent pain nerve endings. Triphala has clearly shown analgesic activity in rats using experimental models.

It was also found that higher doses of aloe vera were effective as an analgesic in the models functional for study of somatic pain. Aloe Vera produced significant results as analgesic in the hot plate method.

CONCLUSION

From the above study we can conclude that the drug selected can be used as alternative analgesic for conventional NSAID's for better tolerability and less side effects.

REFERENCES

1. Clark CRA: Neurological Diseases. In: Parveen K and Michael C (eds) Clinical Medicine. W.B saunders. 2001; 1035- 1036.
2. Smyth EM, Grosser T and FitzGerald GA. Goodman & Gilman's The Pharmacological basis of therapeutics. 12th ed. New York: McGraw-Hill Companies Inc. Chapter 33, Lipid-Derived Autocoids: Eicisanoids and Platelet-Activaing Factor. 2011; 937-55.
3. WHO monographs on selected medicinal plants. Health Organization Geneva. 1999; 1: 33-42.
4. Ely LS, Engroff P, Guiselli SR, Cardoso GC, Morrone FB and Carli GA. Use of anti-inflammatory and analgesic drugs in an elderly population registered with a Family Health Program. Rev. Bras. Geriatr. Gerontol., Rio de Janeiro. 2015; 18(3):475-85.
5. Mishra D, Ghosh G, Kumar PS and Panda PK. An experimental study of analgesic activity of selective COX2 inhibitor with conventional NSAIDS. Asian Journal of Pharmaceutical and Clinical Research. 2011; 4(1):78-81.
6. Cena C, Lolli ML, Lazzarato L, Guaita E, Morini G, Coruzzi G, McElroy S P, Megson I L, Fruttero R and Gasco A. Anti-inflammatory, gastrosparing, and antiplatelet properties of new NO-donor esters of aspirin. J. Med. Chem. 2003; 46: 747.
7. Hardman JG, Limbird LE and Molinoff PA. Analgesic-antipyretic and anti-inflammatory agents and drugs employed in the treatment of gout., 9th ed., The Pharmacological Basis of Therapeutics, McGraw-Hill, New York. 1996; 617.
8. Wolfe MN, Lichtestein DR and Singh GN. Gastrointestinal Toxicity of Non-Steroidal Anti-inflammatory Drugs. N. Engl. J. Med. 1999; 128.
9. Dubois RW, Melmed GY, Laine L and Henning JM. Guidelines for the appropriate use of non-steroidal anti-inflammatory drugs, COX2 Specific inhibitors and proton pump inhibitors in patients requiring Chronic anti-inflammatory therapy. Ailment Pharmacol. Ther. 2004; 19:197.

10. Barua CC, Roy JD, Buragohain B, Barua AG, Borah P and Lahkar M. Analgesic and anti-nociceptive activity of hydroethanolic extract of *Drymaria cordata* Willd. Indian J Pharmacol. 2011; 43:121-5.

11. Manvitha K and Bidya B. Aloe vera: a wonder plant its history, cultivation and medicinal uses. Journal of Pharmacognosy and Phytochemistry 2014; 2(5): 85-8.

12. Grace OM, Buerki S, Symonds MRE, Forest F, Wyk AE, Smith GF et al. Evolutionary history and leaf succulence as explanations for medicinal use in aloes and the global popularity of Aloe vera. BMC Evolutionary Biology 2015; 15: 29.

13. Verma N, Pratap AP, Amresh G, Sahu PK, Singh A and Mishra N. Review on wonderful and miraculous Triphala. J Pharm Res. 2011; 4(3):690-694.

14. Majumdar A. Ayurveda: The Ancient Science of Healing, MacMillan India Ltd. New Delhi, India. 2004; 2.